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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GODDARD, LAURA B	
ART UNIT	PAPER NUMBER
1642	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/579,500	MEHTA ET AL.	
	Examiner	Art Unit	
	LAURA B. GODDARD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *55-111* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *55,57,61,63,65,67,69,71-74,78,80,82,84,86,88,90-93,97,99 and 101* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 May 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/18/06, 6/26/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 56,58-60,62,64,66,68,70,75-77,79,81,83,85,87,89,94-96,98,100 and 102-111.

DETAILED ACTION

1. The response filed on September 4, 2009 to the restriction requirement of August 6, 2009 has been received. Applicant has elected the species of "a method comprising steps a and b using a single reporter protein," "a cell," and "SEQ ID NO:4" for examination. Claims 55-111 are pending. Claims 56, 58-60, 62, 64, 66, 68, 70, 75-77, 79, 81, 83, 85, 87, 89, 94-96, 98, 100, and 102-111 are withdrawn as being drawn to non-elected species. Claims 55, 57, 61, 63, 65, 67, 69, 71-74, 78, 80, 82, 84, 86, 88, 90-93, 97, 99, and 101 are currently under prosecution as drawn to the elected species.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 55, 57, 61, 63, 65, 67, 69, 71-74, 78, 80, 82, 84, 86, 88, 90-93, 97, 99, and 101 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 55 and 57 recite the limitation "**the** Her-2 3' UTR" in part a (claim 55) and the preamble, part a, and part b (claim 57). There is insufficient antecedent basis for this limitation in the claim.

Claim 57 recites the limitation "**the** translational repression of an uORF" in the preamble. There is insufficient antecedent basis for this limitation in the claim.

Claims 67 and 86 recites the limitation "**the** Her-2 5' UTR" in the preamble. There is insufficient antecedent basis for this limitation in the claim.

Deletion of "the" may obviate the rejection.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 55, 57, 61, 63, 65, 67, 69, 71-74, 78, 80, 82, 84, 86, 88, 90-93, 97, 99, and 101 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for screening candidate compounds for a compound that modulates untranslated region (UTR)-dependent expression of Her-2 or a method for screening candidate compounds for a compound that reduces or inhibits the ability of Her-2 3' UTR to override the translational repression of an uORF, comprising:
a. contacting a compound with a mammalian cell engineered to express a reporter protein encoded by a nucleic acid molecule comprising: (i) a first UTR comprising an upstream open reading frame (uORF) Her2 5'UTR (SEQ ID NO:6) or Ship-2, (ii) a reporter gene coding sequence, and (iii) a second UTR comprising SEQ ID NO: 1, wherein the first UTR is upstream of the reporter gene coding sequence and the second UTR is downstream of the reporter gene coding sequence, and wherein the nucleic acid molecule does not comprise SEQ ID NO:3 or 4, and b. detecting the amount or activity of the reporter protein, wherein a change in the amount or activity of the reporter protein

in the presence of the compound relative to the amount or activity of the reporter protein in the absence of the compound indicates that the compound modulates UTR-dependent expression of Her-2, or wherein a decrease in the amount or activity of the reporter protein in the presence of the compound relative to the amount or activity of the reporter protein in the absence of the compound indicates that the compound reduces or inhibits the ability of the Her-2 3' UTR to override the translational repression of an uORF; does not reasonably provide enablement for said methods comprising identifying candidate compounds that reduce or inhibit the ability of Her2 3'UTR to override the translational repression of *any uORF*; methods comprising *any cell;* methods comprising a nucleic acid molecule comprising *any first UTR comprising any uORF;* wherein the *uORF is found anywhere in Her-2 5'UTR;* wherein the uORF is *"a" or any Ship-2 uORF*; or a second UTR comprising *any fragment of SEQ ID NO:1*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single,

simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The specification discloses that in eukaryotes, untranslated regions (UTRs) are important for overall regulation of translation (p. 1). Her2 is an oncogenic protein implicated in several cancers and at least two elements within the Her2 5' UTR have been reported to be strong regulators of polypeptide levels (p. 2). In the examples, the specification discloses making variations of Her2 5' UTR/reporter gene/Her2 3' UTR constructs. The Her2 5'UTR suppresses reporter gene translation but the presence of Her2 3'UTR in the construct overrides the 5'UTR's suppressive effects and increases reporter gene translation (Examples 1-3). The specification discloses that in order to override the 5'UTR's suppressive effects, the Her2 3'UTR must comprise at least SEQ ID NO:1 (Example 5). The specification discloses that SEQ ID NO:1 is a 73 nucleotide fragment of the Her2 3'UTR and is also known as "TRE1" (p. 12). The full length, naturally occurring Her2 3' UTR is represented by SEQ ID NO:3 or 4 (p. 12), however, the term "UTR" refers to any reading frame within mRNA that is not translated (p. 11; p. 21). The specification discloses that Ship-2 mRNA also acts like Her2 5'UTR in that is suppresses reporter gene translation. A construct of Ship-2/reporter gene/Her2 3' UTR,

demonstrated that the Her2 3'UTR was able to override the translational suppressive effects of Ship-2 and increase reporter gene translation (Example 6). Point mutagenesis at the start of uORF in the Her2 5'UTR prevents TRE1-dependent increase in reporter protein expression level (Example 7). The Her2 5'UTR is represented by SEQ ID NO:6 (p. 12).

One cannot extrapolate the disclosure of the specification to the scope of the claims because the specification does not provide guidance or examples for screening assays that identify compounds that modulate UTR-dependent expression of Her-2 or that reduce or inhibit the ability of Her-2 3'UTR to override the transcriptional repression of **any uORF** comprising using **any first UTR comprising any uORF**, comprising **"a" or any sequence of Ship-2 uORF**, or a second UTR comprising **any fragment of SEQ ID NO:1**. The specification discloses only constructs comprising Her2 5'UTR (SEQ ID NO:6) or Ship-2/ reporter protein/ Her-2 3'UTRs comprising SEQ ID NO:1 that function to produce reporter protein activity or reporter protein amounts that are measurable and can be used predictably in the claimed assays. The specification discloses that the construct will not predictably function to produce or translate reporter proteins unless the Her2 3'UTR in the construct comprises at least SEQ ID NO:1 (Examples 5 and 6), therefore one of skill in the art could not predictably use the broadly claimed construct to screen for candidate compounds as claimed unless the construct comprises a downstream Her2 3'UTR comprising all of SEQ ID NO:1. The specification further discloses that mutations in the uORF of Her2 5'UTR prevent the Her2 3'UTR from overriding the translational suppressive effects of the Her2 5'UTR, hence any uORF's or

any first UTRs would not predictably produce reporter protein and function as claimed because altering sequences or structure disrupts function and reporter protein translation. Therefore one of skill in the art could not predictably use the broadly claimed construct for screening candidate compounds unless the construct comprises an upstream first UTR that is Her2 5'UTR or comprises the uORF Ship-2. A high quantity of experimentation would be required to determine which first UTR or uORF and which fragments of SEQ ID NO:1 would predictably function as claimed.

One cannot extrapolate the disclosure of the specification to the scope of the claims because the specification does not provide guidance or examples for the claimed methods predictably functioning in **any cell** other than a mammalian cell. The specification only exemplifies expressing the claimed construct in mammalian cells. Those of skill in the art recognize that other cells, such as plant cells, lack mammalian cell machinery and proteins that play a critical role in 3' and 5'UTR translational function, therefore one of skill in the art could not predictably use any cell as broadly claimed to screen for candidate compounds that modulate UTR-dependent expression of Her-2 or reduce or inhibit the ability of Her-2 3'UTR to override the translational repression of an uORF.

Finally, one cannot extrapolate the disclosure of the specification to the scope of the claims because the specification does not provide guidance or examples for any construct that "does not comprise the Her-2 3' UTR." The specification discloses full length, naturally- occurring Her2 3' UTRs SEQ ID NOs:3 and 4, however, the specification further discloses that UTRs can be any region of mRNA that is not

translated into protein (p. 11) and can comprise one or more regulatory elements that modulate untranslated region-dependent regulation of gene expression (p. 21). The specification also identifies several variants of Her-2 3'UTRs as "3' UTR" in the figures and examples. Therefore, according to the specification, any Her-2 3'UTR comprising SEQ ID NO:1 or fragments would also be a "Her-2 3'UTR" hence the claim contradicts itself because the claim requires SEQ ID NO:1 or fragments to be comprised in the construct. One of skill in the art could not predictably make and use a construct as claimed because any inclusion of SEQ ID NO:1 or fragments would be a construct comprising a or the "Her-2 3'UTR." Unless the construct comprises the Her-2 3'UTR comprising SEQ ID NO:1, the construct will not function as claimed.

Therefore, in view of the quantity of experimentation necessary, the breadth of the claims, lack of guidance in the specification, and the absence of working examples for the broadly claimed constructs and cells, it would require undue experimentation for one skilled in the art to practice the invention as broadly claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States

only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 55, 57, 61, 63, 65, 67, 69, 71-74, 78, 80, 82, 84, 86, 88, 99-93, 97, 99, and 101 are rejected under 35 U.S.C. 102(e) as being anticipated by WO 2004/065561, Cao et al, filed January 21, 2004 claiming priority to January 21, 2003.

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Cao et al teach a method for identifying compounds that modulate the UTR-dependent expression of a target gene, comprising contacting a compound with a cell genetically engineered to express a nucleic acid comprising a reporter gene operably linked to one or more UTRs, preferably the 5'UTR and 3'UTR of a target gene, and measuring the expression of the reporter gene ([0095]; section 5.4), wherein the target gene is ERBB2, also known as Her-2 (p. 34, [00101]; p. 40, [00102]; section 6.28), or is SHIP-2 (p. 35, [00101]), wherein the reporter gene encodes luciferase protein (p. 54, section 5.2.1.1), wherein the nucleic acid comprises a first UTR comprising uORF Her2 5'UTR, reporter gene luciferase, and a second UTR comprising Her2 3'UTR, and wherein the cell is a cancer cell, or breast cancer cell MCF-7 that expresses Her2 (p. 163-164, [0471-0477], sections 9.1.2 to 9.3).

The reference does not specifically teach that the Her2 5'UTR is SEQ ID NO:6, however, the claimed Her2 5'UTR appears to be the same as the prior art Her2 5'UTR, absent a showing of unobvious differences. Further, the reference does not specifically teach that the nucleic acid molecule does not comprise "the Her2 3'UTR," however, given it is unclear which Her2 3'UTR is "the 3'UTR" the claimed Her2 3'UTR appears to be the same as the prior art Her2 3'UTR, absent a showing of unobvious differences. With regards to claims 82 and 101, given the Her2 3'UTR can be either SEQ ID NO:3 or 4, it is expected that the Her2 3'UTR of the prior art would not comprise at least one of SEQ ID NO:3 or 4. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

The "wherein" clauses of claims 55, 57, 61, and 63 state the intended result of the step of detecting the amount or activity of the reporter protein. The wherein clause does not require steps to be performed and does not limit the claim to a particular structure, therefore is not given weight. See MPEP 2111.04.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the

unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 55, 57, 61, 63, 65, 67, 71-74, 78, 80, 82, 84, 86, 90-93, 97, 99, and 101 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-93 of copending **Application No. 10/895,393**. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are claiming common subject matter. The claims of both the copending and instant application are drawn to a method for screening candidate compounds for a compound that modulates untranslated region (UTR)-dependent expression of a target gene comprising: a. contacting a compound with a cell engineered to express a reporter protein encoded by a nucleic acid molecule comprising: (i) an upstream 5' UTR comprising an upstream open reading frame (uORF), (ii) a reporter gene coding sequence, and (iii) a downstream 3' UTR, and b. detecting the amount or activity of the reporter protein, wherein the cell is a cancer cell,

wherein the reporter protein is luciferase. Application 10/895,393 teaches that the target gene can be Her2 and teaches the Her2 5'UTR (SEQ ID NO:17) and 3'UTR of Her2 that consists of instant SEQ ID NO:1, the 73 nucleotide fragment of Her2 3'UTR (see SEQ ID NO:22, paragraph [47]). Application 10/895,393 teaches that the cell can express Her2 ([0218]).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

6. **Conclusion:** No claim is allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAURA B. GODDARD whose telephone number is (571)272-8788. The examiner can normally be reached on 7:00am-3:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Laura B Goddard/
Primary Examiner, Art Unit 1642